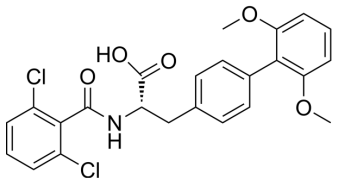
TR-14035

Cat. No.:	HY-15770
CAS No.:	232271-19-1
Molecular Formula:	$C_{24}H_{21}Cl_2NO_5$
Molecular Weight:	474.33
Target:	Integrin
Pathway:	Cytoskeleton
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 41 mg/mL (86.44 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1082 mL	10.5412 mL	21.0824 mL
	5 mM	0.4216 mL	2.1082 mL	4.2165 mL
	10 mM	0.2108 mL	1.0541 mL	2.1082 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TR-14035 is a orally active dual $\alpha_4\beta_7/\alpha_4\beta_1$ integrin antagonist, with IC_{50} s of 7 nM and 87 nM for $\alpha_4\beta_7$ and $\alpha_4\beta_1$, respectively. TR-14035 can be used for the research of inflammation and autoimmune diseases[1][2].

IC_{50} & Target

α4β7	α4β1
7 nM (IC_{50})	87 nM (IC_{50})

In Vitro

TR14035 blocks adhesion of RPMI-8866 cells to MAdCAM-Ig by 100% at 1 μM, with an approximate IC_{50} of 0.01 μM[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

TR-14035 (3?mg/kg; i.g.) produces a significant decrease of the airways hyper-responsiveness to 5-hydroxytryptamine (5-HT) in an experimental model of allergic asthma in Brown Norway rats[3].

?TR-14035 exhibits moderate oral bioavailability (rat 17.1%, dog 13.2%) and C_{max} (rat 0.18, dog 0.10 μg eq./mL) following oral administration (rat 10 and dog 10 mg/kg)[4].

?TR-14035 exhibits terminal elimination half-lives (rat 0.28 h and, dog 0.81 h) due to high plasma clearance (3865 and 1664 mL/h/kg respectively) following intravenous administration (rat 3 mg/kg and dog 3 mg/kg)[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Brown Norway rats (250-300 g)[3]
Dosage:	3 mg/kg
Administration:	Oral gavage, 1 h before and 3 h after antigen challenge
Result:	Suppressed antigen-induced airway hyper-responsiveness and inflammation.

Animal Model:	Male Sprague-Dawley rats (250-320 g)[4]
Dosage:	3 mg/ kg for i.v.; 10 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	Oral bioavailability (17.1%), C_{max} (0.18 μg eq./mL), $T_{1/2}$ (0.28 h).

Animal Model:	Male beagle dogs[4]
Dosage:	3 mg/kg for i.v.; 10 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	Oral bioavailability (13.2%), C_{max} (0.10 μg eq./mL), $T_{1/2}$ (0.81 h).

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Dec 17;116(51):25860-25869.
- Obesity. 2015 Apr;23(4):779-85.
- FASEB J. 2021 Feb;35(2):e21282.
- PLoS One. 2016 Feb 3;11(2):e0148333.

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REFERENCES

[1]. Sircar I, et al. Synthesis and SAR of N-benzoyl-L-biphenylalanine derivatives: discovery of TR-14035, a dual alpha(4)beta(7)/alpha(4)beta(1) integrin antagonist. Bioorg Med Chem. 2002 Jun;10(6):2051-66.

[2]. Egger LA, et al. Alpha(4)beta(7)/alpha(4)beta(1) dual integrin antagonists block alpha(4)beta(7)-dependent adhesion under shear flow. J Pharmacol Exp Ther. 2002 Jul;302(1):153-62.

[3]. Julio Cortijo, et al. A small molecule, orally active, α4β1/α4β7 dual antagonist reduces leukocyte infiltration and airway hyper-responsiveness in an experimental model of allergic asthma in Brown Norway rats. Br J Pharmacol. 2006 Mar; 147(6): 661–670.

[4]. M Tsuda-Tsukimoto, et al. Pharmacokinetics and metabolism of TR-14035, a novel antagonist of a4ss1/a4ss7 integrin mediated cell adhesion, in rat and dog. Xenobiotica

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